



## When Should the Labor Induction be Started For Late-term Pregnancies, in the Morning or in the Evening?

### Geç-Term Gebelikler için Doğum İndüksiyonu Ne Zaman Başlatılmalı, Sabah mı ya da Akşam mı?

Morning or Evening Induction of Labor

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#### Özet

**Giriş:** İntravenöz oksitosin infüzyonu ile doğum indüksiyonu sabah ya da akşam başlatılan geç-term gebeliklerin sonuçlarını incelemek. **Gereç ve Yöntem:** Sefalik prezantasyonda tekil gebeliğe sahip, gebelik yaşı 41 0/7 haftadan 41 6/7 haftaya kadar olan 266 tane gebe bu retrospektif çalışmaya katılmıştır. İntravenöz oksitosin ile doğum indüksiyonları sabah saatlerinde (08.00-12.00) ya da akşam saatlerinde (16.00-20.00) başlatılmıştır. Doğum sonuçları ve gece saatlerindeki (20.00-08.00) doğumlar kaydedilmiştir. **Bulgular:** Primipar gebelerde, doğum eylemi süresi, doğum eyleminin aktif faz uzunluğu akşam grubunda sabah grubuna göre anlamlı olarak daha kısaydı. Multipar gebelerde, gece saatlerinde doğum oranı akşam grubunda sabah grubuna göre anlamlı derecede daha fazla idi. Ayrıca gece saatlerinde doğum, yenidoğan yoğun bakım ünitesine başvurmak için anlamlı bir risk faktörü olarak bulundu. **Tartışma:** İntravenöz oksitosin infüzyonu ile akşam başlatılan doğum indüksiyonu, primipar gebelerde doğum eylemi süresini kısaltırken multipar gebelerde kısaltmaz. Gece saatlerindeki doğum kötü perinatal sonuç için risk faktörü olabilir. Doğum indüksiyonu planlanırken, parite, indüksiyon başlama zamanı ve tahmini doğum saati olası kötü neonatal sonuçları azaltmak için dikkate alınmalıdır.

#### Anahtar Kelimeler

Doğum İndüksiyonu; Oksitosin; Sabah; Akşam

#### Abstract

**Aim:** We aimed to investigate the labor outcomes of late-term pregnancies underwent intravenous oxytocin induction starting in the morning compared with starting in the evening. **Material and Method:** 266 women with a singleton pregnancy in cephalic presentation, at gestational age of 41 0/7 through 41 6/7 weeks were enrolled in this retrospective study. Labor inductions with intravenous oxytocin were started in the morning hours (08.00-12.00) or in the evening hours (16.00-20.00). Labor outcomes and night-time (20.00-08.00) deliveries were recorded. **Results:** In primiparae group, labor duration and active phase length of labor were significantly shorter in the evening group than in the morning group. In multiparae women, the ratio of night-time delivery was significantly higher in evening group as compared to morning group. And also night-time delivery was found as a significant risk factor for neonatal intensive care unit admission. **Discussion:** Induction of labour with intravenous oxytocin starting in the evening shortens labor duration in primiparae women, but not in multiparae women. Night-time delivery may be a risk for poor perinatal outcome. As the labor induction is planned, parity, start time of induction and estimated delivery time should be taken into account to reduce the risk of poor neonatal outcome in late-term pregnancies.

#### Keywords

Labor Induction; Oxytocin; Morning; Evening

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## Introduction

In 2013, gestational period of 41 0/7 through 41 6/7 weeks was defined as late-term pregnancy [1]. At late term pregnancy period and beyond, both mother and baby are at increased risk of adverse events. Thus, most clinicians prefer to induce labor after 41 weeks of gestation [2-3]. Many different methods are used for the induction of labor according to cervical characteristics. Among these protocols, induction with intravenous oxytocin is often carried out as the cervix is favourable (usually a Bishop score of six or more) [3].

Due to the personal availability, obstetricians generally plan to deliver pregnant women during office hours. Therefore, they often start the labor induction early in the morning of the working day [4]. However, it has been shown that spontaneous onset of labor has a circadian rhythm in which the labor starts in the evening. And also the labor duration shortens as the labor contractions start in the evening [5]. Because of this, in late term pregnancies, starting induction of labor in the evening, coinciding with the circadian rhythm of natural birth, might be more beneficial for both mother and baby. So, we performed a retrospective study of late-term pregnancies to investigate the outcomes of induced labor with intravenous oxytocin with a start in the morning compared with a start in the evening.

## Material and Method

This retrospective study was carried out at Zekai Tahir Burak Woman's Health Education and Research Hospital. This is a tertiary referral research hospital located in the central region of Turkey. Two hundred and sixty-six pregnant women with a singleton pregnancy in cephalic presentation, at gestational age of 41 0/7 through 41 6/7 weeks were enrolled in this study. All of them underwent labor induction with intravenous oxytocin infusion in the department of obstetrics between January 2014 and March 2014 due to late-term pregnancy. Ethical permission was obtained from the regional ethics committee of hospital. Data were collected from hospital records. Gestational age was established by the last menstrual period and confirmed by first trimester sonography for all women. Maternal age, gravidity, parity, body mass index and birth weight of newborn were the demographic variables. All women did not have any contraindications for labor induction. Time for the start of induction was in the morning hours (08.00-12.00) or in the evening hours (16.00-20.00). Before the start of induction, all women had favourable cervix (Bishop score  $\geq 6$ ) for intravenous oxytocin induction, reassuring fetal heart rate (FHR) pattern obtained by external heart rate monitoring and estimated fetal weight of  $< 4000$ g with normal amniotic volume on ultrasonography. Women with any systematic diseases, previous uterine incision, premature membrane ruptures, previous cervical ripening, cervical dilation of 3cm or greater and uterine contractions greater than or equal to 3 instances in 10 minutes and who were smokers were excluded.

Oxytocin was administered in the same way for all women as slow intravenous infusion (5 IU) in 500 ml of 5% isotonic glucose solution. Infusion speed was strictly controlled by a infusion pump and adjusted to the uterine response, starting with a dose of 0.1 at 0.4 ml/minute with a maximum flow of 2 ml/minute. Infusion flow was increased incrementally over 15-30 minute,

according to uterine activity and fetal tolerance. When uterine activity reached an appropriate level (3-5 contractions/10 minute), the flow was kept at a constant level to maintain labor. Each hour during labor, a senior obstetrician performed a vaginal examination. When cervical dilation reached 5 cm or more, artificial rupture of membranes was performed at the discretion of the physician.

For all pregnant women, the starting time for labor induction and the time of delivery were recorded. Labor duration, active phase length of labor and number of night-time delivery were the primary outcomes of the study. Labor duration was defined as the time between the start of induction and the time of birth. Active phase length was defined as the start of regular contractions every 3-4 minutes with 5 cm of cervical dilation to delivery. We defined night-time delivery as delivery between 20.00 and 08.00.

Several obstetrical and perinatal data were retrieved from the obstetrical records as secondary outcome measures. Rate of uterine hyperstimulation (defined as 5 or more contractions in 10 minutes or contractions lasting more than 90 seconds to 2 minutes [6-7]), duration of third phase of labor, delivery modes (no instrumental delivery was performed during the study period) were recorded. Fetal distress during induction of labor was defined when non reassuring FHR patterns including repeated late decelerations and/or severe variable decelerations, prolonged deceleration, tachycardia, or reduced variability were detected by external fetal heart monitoring. Two neonatal outcomes were also analyzed: Rate of apgar score at 5 minute  $< 7$  and rate of admission to neonatal intensive care unit (NICU).

Statistical analysis was performed using the Statistical Program for Social Sciences (SPSS, Version 15.0; Chicago, IL, USA). The normal distribution of the variables was analyzed by the Kolmogorov-Smirnov test. Continuous variables with normal distribution are presented as mean  $\pm$  standard deviation. Median (minimum-maximum) value is used where normal distribution is absent. Quantitative variables are given as number (percentage). Statistical comparison was carried out by Chi-square ( $\chi^2$ ), Mann-Whitney and Independent sample t tests where appropriate. Logistic regression model was performed to analyze risk factors for NICU admission. The sample size was determined according to the results of the central limit theorem [8].  $P < 0.05$  was considered statistically significant.

## Results

A total of 266 pregnant women were included in this study. Of them, 155 (58.3 %) women were primiparae and 111 (42.7 %) women were multiparae. In the primiparae group, there were 82 women in whom the labor induction was started in the morning and 73 women in whom the induction was started in the evening. In the multiparae group, labor inductions of 63 women were started in the morning while 48 inductions were started in the evening. In our population, there were no significant differences in the maternal characteristics and birthweight of infants, which are recorded in Table 1.

With regard to primary outcome, in primiparae group mean labour duration and active phase length were significantly shorter in evening group ( $10.29 \pm 2.71$ ,  $4.58 \pm 1.06$ , respectively) than in morning group ( $11.33 \pm 2.42$ ,  $6.06 \pm 1.24$ , respectively) ( $p = 0.039$

Table 1. Maternal Characteristics and Birthweight of Infants

	primiparae		p	multiparae		P
	morning (n=82)	evening (n=73)		morning (n=63)	evening (n=48)	
Maternal age (years)	26.16± 2.85	25.64± 2.48	0.235	26.00 ±2.89	26.73 ±2.39	0.159
Parity	0	0	---	2 (1-4)	2 (1-4)	0.281
BMI (kg/m2)	26.02± 1.59	25.99± 1.58	0.920	26.28±1.48	25.87±1.69	0.184
Gestational age (days)	289.54± 1.92	289.73± 1.94	0.542	289.57 ±1.78	289.58 ±1.84	0.973
Bishop score	6 (6-8)	6 (6-8)	0.461	6 (6-8)	6 (6-8)	0.678
Birthweight (gr)	3420.49 ±428.00	3477.81± 423.13	0.404	3436.19 ±578.63	3598.33± 152.64	0.061

Values were given as mean±standard deviation, median (minimum-maximum) or number (percentage)  
p<0.05 was considered statistically significant

and p<0.001, respectively). However, there was no statistically significant difference in the percentage of women who delivered at night (p=0.405) (Table 2). In multiparae women, the differences of labor duration and active phase length between morning and evening groups were not statistically different (p=0.206 and p=0.874, respectively). But, the percentage of night birth was significantly higher in evening group (81.3%) as compared to morning group (23.8%), among the multiparae (p<0.001)(Table2).

Table 2. Primary and Secondary Outcomes In Primiparae and Multiparae

	Primiparae		p	multiparae		p
	morning	evening		morning	evening	
Primary outcomes						
Labour duration (hours)	11.33±2.42	10.29±2.71	0.039	7.79±1.93	8.22±1.55	0.206
Active phase length (hours)	6.06±1.24	4.58±1.06	<0.001	3.15±0.92	3.09±0.62	0.874
Night-time delivery	23 (28.0)	25 (34.2)	0.405	15 (23.8)	39 (81.3)	<0.001
Secondary outcomes						
Uterine Hyperstimulation	12 (14.6)	4 (5.5)	0.062	2 (3.2)	1 (2.1)	0.729
Third phase length (minutes)	4.04±1.21	5.05±5.75	0.119	4.22±1.05	3.81±1.25	0.064
Cesarean section	26 (31.7)	27 (37.0)	0.489	6 (9.5)	6 (12.5)	0.617
Cesarean section for foetal distress	15 (18.3)	13 (17.8)	0.938	5 (7.9)	5 (10.4)	0.658
Apgar score at 5th minute<7	9 (11.0)	5 (6.8)	0.371	7 (11.1)	4 (8.3)	0.628
NICU admission	7 (8.5)	13 (17.8)	0.086	4 (6.3)	6 (12.5)	0.617

Values were given as mean±standard deviation, median (minimum-maximum) or number (percentage)  
p<0.05 was considered statistically significant

For the secondary outcomes, in both primiparae and multiparae groups, there were no statistically significant differences in terms of the incidence of uterine hyperstimulation during labor, cesarean section, cesarean section for foetal distress, newborn with 5th minute Apgar score ≤7, NICU admission and the length of the third stage of labor (Table 2). In our study, all infants with 5th minute Apgar score ≤7 were admitted to NICU.

When we examined the multivariate effects of parity, starting time of induction and night-time delivery considered to be effective risk factors in predicting NICU admission, night-time delivery was a statistically significant risk factor (OR=3.23, 95% CI:1.40-7.44; p=0.006). However, parity and starting time of induction were not statistically significant risk factors (p=0.116 and p=0.174, respectively) (Table 3).

**Discussion**

In our study, we found two important aspects. First, in primiparae late-term pregnant women, intravenous oxytocin induction

with a starting point in the evening shortens the duration and active phase of labor compared with in the morning. On the other hand, the starting time of labor induction with intravenous oxytocin does not have any impact on the labor duration or active phase length in multiparae women. Second, birth during night-time increases the risk of poor perinatal outcome.

In literature, there is no enough study comparing the effect of starting time of labor induction with intravenous oxytocin infusion on labor duration. In 2009, Bakker et al. [9] designed an only randomised controlled study to compare outcomes of induced labor with intravenous oxytocin with a start in the morning versus in the evening. They randomized 371 pregnant women beyond a gestational age of 36 weeks with a favourable cervix

(Bishop score>6) to either the morning group with a start of induction of labor at 07:00 hours, or the evening group with a start at 21:00 hours. They defined the duration of labor as time between the moment oxytocine was administered or, in case the contractions started spontaneously and the moment of birth. Finally, they concluded that there was no evidence of a difference in labor duration of both primiparae and multiparae subgroups. In contrast to Bakker et al., in primiparae late term women, we have found that labor duration and active phase length of labor is shorter in the evening group than in the morning group. Our results can be explained by cir-

Table 3. Logistic regression model of risk factors in predicting NICU admission

	Wald	p	OR	95% CI
Parity	2.47	0.116	0.51	0.22-1.18
Start time of induction	1.85	0.174	1.76	0.78-3.98
Night-time birth	7.59	0.006	3.23	1.40-7.44

OR: Odds Ratio, CI: Confidence Interval  
p<0.005 was considered statistically significant

cadian rhythm of oxytocin concentration that was documented by human and animal studies [10-15]. Oxytocin concentrations and myometrial oxytocin receptors increase during evening and night time with a decreased estradiol/progesterone ratio. Seeing that, uterine myometrium becomes more sensitive for maternal oxytocine in the evening or night time than during day time and starting induction of labor in harmony with the circadian rhythm of oxytocin shortens the duration of labor. However, this phenomenon is not available for multiparae women. It is possible that uterine myometrium in multiparae women is sensitive to less oxytocin concentrations to complete the labor,

thus oxytocin levels in the morning is proven to be enough for multipare women.

In literature, there are several studies comparing the neonatal outcomes of infants born during night-time or day-time. However, the findings about the birth time on perinatal mortality and morbidity have been inconsistent. Some studies reported increased risks for births during the evening or night, leading to questions about the quality of care provided during night-time [16-20]. But, two retrospective cohort studies including great numbers of deliveries did not find any significant differences in neonatal morbidity or mortality by time of delivery [21-22]. In our study, the risk of NICU admission for infants increased if the birth took place at night. This might be the result of a multiple factors, like diminished numbers of and expertise of staff available, reduced access to diagnostic tests and procedures, a lower degree of supervision of residents, long-duration shifts and tiredness of personnel, delays in availability of necessary personnel in case of emergency.

In the current study, starting of induction in the morning compared with the evening was not associated with statistically significant differences in the number of primiparae or multiparae women who had uterine hyperstimulation during labor, cesarean section, cesarean section for fetal distress, newborns with Apgar score at 5th minute < 7 and NICU. Similarly, Bakker et al. [9] did not report any significant differences between morning and evening induction in terms of cesarean section and newborns with Apgar score at 5th minute < 7. There was also no significant difference reported for neonatal admission between the study groups in the multiparae women. However, among primiparae women, significantly more children born from mothers in the morning group were admitted to the NICU.

Although retrospective design is a weakness for our study, based on the present findings we suggest that starting time of labor induction with oxytocin infusion may alter the duration of labor, especially in primipare women. In addition, night-time delivery seems to be a risk factor for poor perinatal outcome. Accordingly, as delivery is planned, the parity of woman, starting time of the labor induction and estimated birth time should be taken into account to reduce the risk of poor perinatal outcome to a minimum. Further prospective randomised studies are needed about this topic.

### Competing interests

The authors declare that they have no competing interests.

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